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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,247	07/02/2007	Foo Yew Liew	0380-P04195US00	7364

110 7590 04/27/2009

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EXAMINER	
MERTZ, PREMA MARIA	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
04/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,247	LIEW ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/3/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,15 and 17-40* is/are pending in the application.

4a) Of the above claim(s) *1-11 and 18-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12, 15, 17, 32-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claim 16 has been canceled in the amendment filed 10/16/08 and claims 13-14 have been canceled previously. Amended claims 12, 15, 17 and new claims 32-40 (10/16/08) are pending in the instant application. Claims 1-11 and 18-31 are drawn to a non-elected invention.

2. Receipt of applicant's arguments and amendments filed on 10/16/2008 is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 10/16/2008:

(i) the rejection of claims 12, 15-17, under 35 U.S.C. 112, second paragraph.

Applicant's arguments with respect to claims 12, 15, 17, 32-40, have been considered but are moot in view of the new ground(s) of rejection.

4. Applicant's arguments filed on 10/16/08 have been fully considered and were persuasive in part. The issues remaining and new issues are stated below.

Election/Restrictions

5. Applicant's election of Group II (claims 12, 15, 17, 32-40, species: autoimmune disease and subspecies: arthritis) in the reply filed on 3/3/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-8, 9-11 and 18-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claim rejections-35 USC § 112, first paragraph, scope of enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6a. Claims 12, 15, 17, 32-40, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating rheumatoid arthritis or attenuating established arthritis in a subject by administering an effective amount of EBI3-35 to enhance regulatory T cell activity in the subject, does not reasonably provide enablement for a method as recited in claim 12. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

This rejection is maintained for reasons of record set forth at pages 3-8 of the previous Office action of 5/19/2008.

Applicants argue that contrary to the Examiner's assertions, the specification exemplifies treatment of arthritis using the compositions of the invention, at page 27, line 24 over to page 28, line 27, the inventors provide data which indicate that EBI3-35 reduces markers of airway hypersensitivity (cellular infiltrates into bronchial alveolar lavage, eosinophilia, antigen-specific serum IgE, and IL-4 in bronchial alveolar lavage fluid) in an animal model of asthma (see Figure 9) and thus the application provides evidence that EBI3-p35 is effective to modulate the immune response in two rather different conditions (arthritis and asthma), whose pathogenesis shares a very significant involvement of regulatory T cell activity. However, contrary to Applicants

arguments, independent claim 12 encompasses a method to enhance regulatory T cell activity to ameliorate symptoms in "all autoimmune diseases" which can range from Hashimoto's disease to Graves' disease and systemic lupus erythematosus. Furthermore, other than treatment of arthritis, and providing data which indicate that EBI3-35 reduces markers of airway hypersensitivity (cellular infiltrates into bronchial alveolar lavage, eosinophilia, antigen-specific serum IgE, and IL-4 in bronchial alveolar lavage fluid) in an animal model of asthma (see specification, page 27, line 24 over to page 28, line 27 and Figure 9), the specification fails to provide any guidance for the successful enhancement of regulatory T cell activity and subsequent amelioration of symptoms of all autoimmune diseases, including autoimmune diseases such as multiple sclerosis.

The amelioration of symptoms in autoimmune diseases, such as multiple sclerosis, has been the subject of intense study for the past several decades. Many promising treatments and therapies have been identified via in vitro experiments, and have not lived up to expectations when tested in vivo. In fact, the number of such treatments, which have failed to live up to their promise exceeds those, which have been performed as hoped by orders of magnitude. The disclosure fails to teach one of ordinary skill in the art a method of ameliorating symptoms in an autoimmune disease such as multiple sclerosis by administering EBI3-p35. It would not be reasonable to expect the claimed product to be effective in the various types of autoimmune diseases. Thus, it would require undue experimentation on the part of the skilled artisan to use the claimed method for treated as recited, in the absence of sufficient information to predict the results with an adequate degree of certainty. In view of this unpredictability in the treatment of multiple sclerosis, there cannot be said to be any reasonable expectation of success at the in vivo

application of a potential therapy for all types of autoimmune diseases, especially in view of the fact that the current specification as filed presents no working examples pertaining to the method of ameliorating symptoms in multiple sclerosis in vivo. Therefore, a method of ameliorating symptoms in an autoimmune disease such as multiple sclerosis by administering EBI3-p35 as recited in claim 12 has not been enabled by the specification. The recitation of "autoimmune disease" in claim 12, is not commensurate with the scope of the specification. Given the breadth of claim 12 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to practice the claimed invention.

An application must be complete as filed. The instant specification as filed does not provide any guidance or examples that would enable a skilled artisan to practice a method of ameliorating symptoms in multiple sclerosis by administering to a patient EBI3-p35 cytokine as claimed, i.e. the instant specification fails to enable a method of using EBI3-p35 cytokine as a therapeutic agent in a multiple sclerosis patient.

Applicants are reminded that "Argument of counsel cannot take the place of evidence lacking in the record" (*In re Scarbrough*, 182 USPQ 298, 302 (CCPA 1974)).

Claim Rejections - 35 USC § 112, second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12, 15, 17, 32-40, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12, line 5, is vague and indefinite because it recites "….is effective enhance…." rather than the correct "…..is effective to enhance".

Claim 15, line 3 is vague and indefinite because it recites "…condition characterized_ by…" rather than "…condition characterized by…".

Claim 38 recites the limitation "two or more said…." in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 17, 32-37, 39-40 are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim rejections-35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8a. Claims 12, 15, are rejected under 35 U.S.C. 102(b) as being anticipated by Devergne et al. (WO 97/13859)

This rejection is maintained for reasons of record set forth at page 9 of the previous Office action of 5/19/2008.

Applicants argue that claim 12 has been amended to recite a method of administration of a therapeutically effective amount of a composition containing the EBI3/p35 cytokine to a subject in need thereof, the composition being effective to ameliorate the symptoms of an autoimmune or inflammatory condition or effective to prevent or ameliorate allograft rejection in said subject and since Devergne et al. never demonstrate an amelioration of an autoimmune or inflammatory condition, it cannot be said that this reference discloses an identical method. However, contrary to Applicants arguments, Devergne et al. discloses a method for modulating the immune response in a subject by administering EBI3-p35 complex to a subject that has an autoimmune condition (see abstract; see page 4, lines 22-30). The method described in the reference meets the limitations of instant claims 12, 15 because the reference anticipates these claims drawn broadly to a method of modulating the immune response in an autoimmune condition. It would be an inherent property of EBI3-p35 to enhance regulatory T cell activity thereby ameliorating the symptoms of an autoimmune condition. Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent. See MPEP 2112-2112.02.

See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001) in which the Court found that preamble language in claims of patents directed to administration of anticancer drug are expressions of purposes and intended results, and as such are non-limiting, since language does not result in manipulative difference in steps of claims. It

does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure.

While the prior disclosure was silent as to the treatment of specific types of autoimmune conditions, the instant claims merely recite a known result, i.e. a method of enhancing regulatory T cell activity by administering EBI3-p35 complex to a subject. The claimed process is not directed to a new use, it is the same use and it consists of the same method as described by the reference.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9a. Claim 17 is rejected under 35 U.S.C. 103(a) as unpatentable over Devergne et al. (WO 97/13859).

This rejection is maintained for reasons of record set forth at pages 10-11 of the previous Office action of 5/19/2008.

Applicants argue that Devergne et al. reference cannot support the obviousness rejection of claim 17 because the disclosure in Devergne et al. is no more than an invitation to test whether EBI3/p35 functions to modulate the immune response. However, contrary to Applicants arguments, if the Devergne et al. reference disclosed a method of enhancing regulatory T cell activity in arthritis, this rejection over claim 17 would have been a 35 USC 102(b) rejection rather than a 35 USC 103(a) rejection. From the teachings of Devergne et al., it would be *prima facie* obvious to one of ordinary skill in the art to administer the EBI3-p35 protein in an inflammatory/autoimmune condition such as rheumatoid arthritis. One of ordinary skill in the art would have been motivated to do so because the reference teaches on page 4, lines 22-30, discloses "….the EBI3/p35 protein complex is administered to a subject that has an autoimmune condition to ameliorate the autoimmune condition". Thus the artisan would have expected success administering EBI3-p35 for enhancing regulatory T cell activity in a subject for the treatment of arthritis.

Conclusion

No claim is allowed.

Claims 12, 15, 17, 32-40, are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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